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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,373	04/04/2001	Stephen R. Quake	3153/1F534US1	2878

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/826,373	Quake
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 10, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-30, 36-40, and 47-50* is/are rejected.

7) ☒ Claim(s) *31-35, 41-46, and 51-55* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2,3*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group II in Paper No. 0503 is acknowledged. The traversal is on the ground(s) that there is no extra burden to examine the claims of both Group I and II. This is found persuasive and therefore, all pending claims in this application are hereby being examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 4-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is rejected over the recitation of the phrase, "target polynucleotide" on step (a). It is not clear if the target polynucleotide is a part of the polynucleotide sample being detected or it is bigger than the polynucleotide sample or it is a part of another reference polynucleotide or all of them. In absence of a clear definition of "target polynucleotide" either in the specification or in the claim, the metes and bounds of the claims are vague and indefinite.

Claim 4 recites the limitation "the strands" in the first line of step (f). There is insufficient antecedent basis for this limitation in the claim. It should be recited as, "the at least one polynucleotide strand".

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-11, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Caetano-Anolles et al. (PCT International Publication Number WO 95/33853) (December 14, 1995).

Caetano-Anolles et al teach a molecular fingerprinting method for identifying a polynucleotide (Page 14, lines 9-14, and Figure 1) comprising the steps of:

a) identifying a target poynucleotide (Figure 1, Panels C and D, and Page 15, lines 8-11);

b) selecting at least one fragment of the target polynucleotide, wherein the fragment is a fixed distance from the restriction site, to generate a set of one or more polynucleotide fragments (Page 20, lines 6-17);

c) designating some or all of the set of fragments as a fingerprint corresponding to the target polynucleotide (Page 20, 18-20);

d) synthesizing one or more oligonucleotide probes to complement the set of polynucleotide fragments (Page 22, line 4 to page 25, line 2);

e) combining the probes, a polynucleotide sample, nucleotide triphosphates, and polymerase to synthesize at least one polynucleotide strand (Page 25, line 3 to page 30, line 17);

f) cutting the strands with restriction enzymes to yield a set of sample fragments of fixed length (Claim 20);

g) comparing the set of sample fragments to the fingerprint (Figures 1-4, and Claim 23).

Caetano-Anolles et al teach a method, wherein each fragment is selected at random (Figure 1, and Page 14, lines 10-14).

Caetano-Anolles et al teach a method, wherein the polynucleotide sample is digested before the combining step with a six-base cutter digestion enzyme (Page 20, line 6 to page 21, line 5).

Caetano-Anolles et al teach a method, wherein the polynucleotide sample is digested into fragments of tens of thousands of base pairs and fragment sizes are determined by gel elctrophoresis (Figures 1-3).

Caetano-Anolles et al teach a method, wherein the nucleotide triphosphates are fluorescently labeled (Page 17, first paragraph).

6. Claims 1-8, 10, 11, 13, 15-17, 20, 36-37, 40, and 47-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Tatari et al. (Proc. Natl. Acad. Sci. USA, (1995), Vol. 92, pages 8803-8807).

Tatari et al. teach a molecular fingerprinting method for identifying a polynucleotide (Abstract) comprising the steps of:

a) identifying a target poynucleotide (Abstract and MATERIALS AND METHODS Section, Population Subsection);

b) selecting at least one fragment of the target polynucleotide, wherein the fragment is a fixed distance from the restriction site, to generate a set of one or more polynucleotide fragments (MATERIALS AND METHODS Section, DNA preparation Subsection);

c) designating some or all of the set of fragments as a fingerprint corresponding to the target polynucleotide (MATERIALS AND METHODS Section, HLA-C locus-Specific Primers Subsection);

d) synthesizing one or more oligonucleotide probes to complement the set of polynucleotide fragments (MATERIALS AND METHODS Section, HLA-C locus-Specific Primers Subsection);

e) combining the probes, a polynucleotide sample, nucleotide triphosphates, and polymerase to synthesize at least one polynucleotide strand (MATERIALS AND METHODS Section, PCR Amplification Subsection);

f) cutting the strands with restriction enzymes to yield a set of sample fragments of fixed length (MATERIALS AND METHODS Section, Digestion with Restriction Endonucleases Subsection and Figure 1);

g) comparing the set of sample fragments to the fingerprint (MATERIALS AND METHODS Section, Agarose Gel Electrophoresis Subsection).

Tatari et al. teach a method, wherein each fragment is selected at random (MATERIALS AND METHODS Section, DNA preparation Subsection).

Tatari et al. teach a method, wherein each fragment is about 20 to about 50 base pairs in length (Table 1).

Tatari et al. teach a method, wherein the sample fragments are compared to the fingerprint by determining the sizes of the sample fragments in relation to the fingerprint fragments (MATERIALS AND METHODS Section, Agarose Gel Electrophoresis Subsection).

Tatari et al. teach a method, wherein the polynucleotide sample is digested after the combining step (MATERIALS AND METHODS Section, Digestion with Restriction Endonucleases Subsection and Figure 1).

Tatari et al. teach a method, wherein the target polynucleotide is associated with a disease (Introduction and Discussion Section, last paragraph).

Tatari et al. teach a method for detecting a particular nucleic acid in a sample, which particular nucleic acid has at least one restriction site (Figure 1), and which method comprises:

a) contacting the sample with a primer that hybridizes to the particular nucleic acid a predetermined distance from the restriction site, a polymerase and a plurality of nucleotides, so that a complementary nucleic acid is synthesized from the primer at least to the restriction site (MATERIALS AND METHODS Section,PCR Amplification Subsection);

b) contacting the complementary nucleic acid with a restriction enzyme under conditions capable of cutting the complementary nucleic acid at the restriction site (MATERIALS AND METHODS Section, Digestion with Restriction Endonucleases Subsection and Figure 1); and

c) detecting a nucleic acid fragment having a particular length equal to the fixed distance (MATERIALS AND METHODS Section, Agarose Gel Electrophoresis Subsection),

wherein the presence of the nucleic acid fragment in the sample indicates that the particular nucleic acid is present in the sample (Results Section, Additional Alleles Predicted by Unusual Restriction Pattern Subsection).

Tatari et al. teach a method, wherein the primer comprises an oligonucleotide about 20-50 nucleotides in length (Table 1).

Tatari et al. teach a method in which no more than a single complementary nucleic acid is synthesized (Table 1 and MATERIALS AND METHODS Section, HLA-C locus-Specific Primers Subsection).

Tatari et al. teach a method, wherein the nucleic acid fragment is detected according to a method that comprises:

I) sorting polynucleotide molecules in the sample according to size by gel electrophoresis (MATERIALS AND METHODS Section, Agarose Gel Electrophoresis Subsection); and

ii) identifying a polynucleotide having the particular length (MATERIALS AND METHODS Section, Agarose Gel Electrophoresis Subsection).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 9, 12, 18, 19, 21-28, 30, 38, 39 and 50 are rejected under 35 U.S.C. 103(a) as being obvious over Tatari et al. (Proc. Natl. Acad. Sci. USA, (1995), Vol. 92, pages 8803-8807) in view of Goodwin et al. (Nucleic Acids Research, (1993), Vol. 21(4), pages 803-806).

Tatari et al teaches the method of claims 1-8, 10, 11, 13, 15-17, 20, 36-37, 40, and 47-48 as described above.

Tatari et al do not teach a method, wherein at least some of the plurality of nucleotides are detectably and fluorescently labeled.

Goodwin et al. teach a method, wherein at least some of the plurality of nucleotides are detectably and fluorescently labeled (Abstract and MATERIALS AND METHODS section).

Tatari et al does not teach the method in which polynucleotides are sorted one at a time in a microfluidic device.

Goodwin et al. teach the method in which polynucleotides are sorted one at a time in a microfluidic device (Abstract, and MATERIALS AND METHODS section, and Figures 1-2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method in which polynucleotides are sorted in a microfluidic device of Goodwin et al. in the method of Tatari et al. since Goodwin et al state, "Sizing of DNA fragments by this approach is much faster, requires much less DNA, and can potentially analyze large fragments with better resolution and accuracy than with gel-based electrophoresis (Abstract, last sentence)". An ordinary practitioner would have been motivated to combine and substitute the method in which polynucleotides are sorted in a microfluidic device of Goodwin et al. in the method of Tatari et al. in order to achieve the express advantages, as noted by Goodwin et al., of a method of sizing DNA fragments which is much faster, requires much less DNA, and can potentially analyze large fragments with better resolution and accuracy than with gel-based electrophoresis.

9. Claim 14 is rejected under 35 U.S.C. 103(a) as being obvious over Tatari et al. (Proc. Natl. Acad.Sci. USA, (1995), Vol. 92, pages 8803-8807) in view of Kanter et al. (Journal of Forensic Sciences, (1986), Vol. 31(2), pages 403-408).

Tatari et al teaches the method of claims 1-8, 10, 11, 13, 15-17, 20, 36-37, 40, and 47-48 as described above.

Tatari et al does not teach the method, wherein the sample polynucleotide is a forensic sample.

Kanter et al. teach the method, wherein the sample polynucleotide is a forensic sample (Abstract, and MATERIALS AND METHODS section, and Figures 1-3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the sample polynucleotide is a forensic sample of Kanter et al. in the method of Tatari et al. since Kanter et al states, "This article presents methods for isolating high molecular weight DNA from dried bloodstains and for subsequent analysis using two probes that recognize high polymorphic regions of human DNA. The experiments demonstrate the feasibility of matching the polymorphic patterns of DNA recovered from a blood stain with the DNA patterns obtained from a blood sample drawn from a suspected individual (Page 403, line 14 to page 404, line 2)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the sample polynucleotide is a forensic sample of Kanter et al. in the method of Tatari et al. in order to achieve the express advantages, as noted by Kanter et al., of an invention which provides methods for isolating high molecular weight DNA from dried bloodstains and for subsequent analysis using two probes that recognize high polymorphic regions of human DNA, and which also demonstrates the feasibility

of matching the polymorphic patterns of DNA recovered from a blood stain with the DNA patterns obtained from a blood sample drawn from a suspected individual.

10. Claims 29 and 49 are rejected under 35 U.S.C. 103(a) as being obvious over Tatari et al. (Proc. Natl. Acad.Sci. USA, (1995), Vol. 92, pages 8803-8807) in view of Langmore et al. (U.S. Patent 6,117,634) (September 12, 2000).

Tatari et al teaches the method of claims 1-8, 10, 11, 13, 15-17, 20, 36-37, 40, and 47-48 as described above.

Tatari et al does not teach the method in which polynucleotide molecules are sorted by HPLC.

Langmore et al. teach the method in which polynucleotide molecules are sorted by HPLC. (Column 18, lines 15-26).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method in which polynucleotide molecules are sorted by HPLC of Langmore et al. in the method of Tatari et al. since Langmore et al states, "Size fractionation can also be achieved by flow of solution through chromatographic media by the techniques of HPLC and FPLC. The ability to fractionate DNA according to length is not affected by the presence of nicks in the double-stranded DNA (Column 18, lines 22-26)". An ordinary practitioner would have been motivated to combine and substitute the method in which polynucleotide molecules are sorted by HPLC of Langmore et al. in the method of Tatari et al. in order to achieve the express advantages, as noted by Langmore et al., of size fractionation that

can also be achieved by flow of solution through chromatographic media by the techniques of HPLC and FPLC and which provides the ability to fractionate DNA according to length not affected by the presence of nicks in the nucleic acid molecule.

Allowable Subject Matter

11. Claims 31-35, 41-46, and 51-55 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau, whose telephone number is (703) 605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti

Patent Examiner

Art Unit 1634

May 15, 2003

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER